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(54) Title: COMESTIBLE CAPSULES HAVING FLAVOURED COATINGS

(57) Abstract

A coated capsule is disclosed comprising a gelatin shell with a flavoured coating. A sugar or sugar substitute is included in the material of the shell and that of the coating to stabilise both compositions and the junction therebetween.

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COMESTIBLE CAPSULES HAVING FLAVOURED COATINGS

This invention relates to comestible capsules for oral administration, and particularly such capsules having flavoured or sweetened coatings. The invention is also concerned with such capsules which are intended for swallowing substantially intact, for release of the contents only when the capsule has reached the stomach.

Many medicines are relatively unpleasant to taste, and in either tablet or encapsulated form, are masked by flavoured coatings to make them more palatable. The present invention is concerned with the provision of a flavoured coating around a gelatin capsule containing a fill composition which is typically liquid, but may be paste like or even solid in some circumstances. Gelatin shells provide a useful means for encapsulating such compositions, but there are problems in applying flavoured coatings thereover. Particularly, typical coatings can provoke changes in the gelatin shell structure which can adversely affect the integrity of the capsule, and in some cases also the coating.

Typical gelatin shells used to encapsulate products comprise gelatin in combination with a plasticiser such as glycerine which, together with water preserve a degree of softness and flexibility in the shell material. Such shells are relatively easy to handle, but have disadvantages in terms of taste. This is particularly relevant to breath fresheners and, according to one aspect of the invention, a breath freshener is provided in the form of a filled gelatin capsule to which is applied a flavoured coating. Such a coated capsule is especially suitable for swallowing prior to rupture of the capsule, whereby the capsule fill is not released until the capsule shell is broken down in the stomach.

For the above and other embodiments according to the present invention, the capsule shell formulation may be adapted, and a flavoured coating applied to the

capsule such that at least at the boundary between them, a stable bond is formed. This enables a substantially dry coating to be created which does not draw the water or plasticiser from the gelatin shell, with the resultant adverse consequences on the shell structure. This can be achieved by including in the capsule shell formulation a sugar or sugar substitute such as sorbitol, and matching it with an equivalent substance in the coating. The effect of this match is to effectively stabilise both the coating and shell formulations and in the gelatin, to prevent the migration of water and glycerine to the coating. In this way, the humectents are retained in the gelatin which can thus preserve its flexibility and palatability if retained in the mouth.

As a general guide, we have established the following ranges of gelatin, glycerine, sugar or sugar substitute and water, as percentages by weight in the shell formulation, to provide a satisfactory base for a coating of for example sorbitol in solution:

Gelatin	33.00 - 58.00
Glycerine	16.00 - 31.00
Sugar or sugar substitute eg Sorbitol	15.00 - 30.00
Water	up to 15.00

Preferably, the ratio of plasticiser (Glycerine + sugar or substitute) to Gelatin is in the range 0.7 to 1.2, preferably 0.8 to 1.0, with the ratio of sugar or substitute to Glycerine in the range 0.8 to 1.2.

We have found that in order to stabilise a soft gelatin shell to which a flavoured coating is to be applied, a relatively high glycerine content must be established with a consequent reduction in the water content. Using sorbitol as the additional component in the shell, and as the basic component for the coating, we have established the following typical minimum levels of glycerine and sorbitol as percentages by weight in the dried shell formulation. The figures for gelatin

and water in the formulation are also given.

Glycerine	17.7
Sorbitol	16.7
Gelatin	56.7
Water	8.9

Total plasticiser: 34.4%;
Plasticiser to Gel ratio: 0.61

The glycerine and sorbitol levels can be further increased with consequential further reduction in the proportions of gelatin, and a typical shell formulation which is able to sustain its softness under an applied flavoured coating of sorbitol is as follows.

Glycerine	21.0
Sorbitol	20.0
Gelatin	50.4
Water	8.6

Total plasticiser: 41.0%
Plasticiser to Gel ratio: 0.81

Experimentation has indicated that the glycerine and sorbitol levels can be increased beyond those quoted above, but we regard the following formulation as demonstrating typical maximum amounts of these components that can be retained in a viable shell structure embodying the invention.

Glycerine	29.3
Sorbitol	28.6
Gelatin	34.5
Water	7.6

Total plasticiser: 57.9%;
Plasticiser to Gel ratio: 1.8

The use of increased glycerine content in gelatin shells to provide improved and stable softness is disclosed in our International Patent Publication No. WO95/00123 to which reference is directed. Formulations

of the kind disclosed in that publication can be used in the exploitation of the present invention, having regard to the above guidance in respect of the additional stabilising component.

While in the above discussion the specified sugar or sugar substitute has been sorbitol, a variety of sugar alcohols or non-reducing saccharides or polyols may be used. For example:

sorbitol; polyglycerol; mannitol; xylitol; maltitol; isomalt; corn syrup, and Anidrisorb (a proprietary mix of sorbitol, sorbitan and mannitol from Roquette Freres).

As noted above, the flavoured coating for products according to the invention is normally based on a sugar or a sugar substitute, and is typically applied to capsules as an aqueous solution in for example, a panning process. Pan coated gelatin capsules are disclosed in British published specification no. 2283899, and products may be coated according to the present invention using the techniques and parameters described therein. The eventual coating will typically be in crystalline form, and as such will tend to draw moisture from the capsule shell. By including water and a sugar or sugar substitute in both the coating material and the shell formulation, when the coating is applied a dynamic balance can be achieved. The coating will normally be applied wet, as in a pan coating process, and this itself assists in stabilising the interface between the coating and shell.

It is of course desirable to minimise the quantity of shell material in the coated product, and in this respect it is recognised that with a sufficiently stable interface and bond between the coating and shell, the coating will serve to reinforce the shell, and the shell to effectively seal the coating. Thus, if the shell thickness can be reduced such that its entire thickness is effectively bonded to the coating, then the resultant

product will include a bare minimum of shell material.

Fill compositions for use in products according to the invention may take many forms, and in this respect reference is directed once again to published British specification no. 2283899. Additionally though, the present invention is suitable for compositions which are not intended to be released in the mouth, but for retention in the capsule until it reaches the stomach. This applies particularly to some breath freshening compositions such as parsley seed oil which can provide a very unpleasant flavour in the mouth despite being effective as a breath freshener from the stomach. The nature of the fill composition can of course have a direct effect on the integrity of the shell material, and oil based compositions such as parsley seed oil can have an additional softening effect on the shell. The presence of a sugar or a sugar substitute such as sorbitol in the shell can also serve to minimise the effect of both oil based and water based fill compositions on the shell.

Example

A breath freshener in the form of a filled capsule embodying the present invention has the following formulations for the fill, shell and coating respectively:

Fill:	Quantity	%age
Aspartame	0.825mg	0.516
Fractionated Coconut oil	66.280mg	41.425
Kaorich Beads	10.888mg	6.8
Levomenthol BP/EP	4.800mg	3.0
Parsley Seed Oil	0.250mg	0.156
Peppermint flavour	6.400mg	4.0
Loders 7(Hard Vegetable Fat)	23.830mg	14.894
Ascorbic Acid	1.500mg	0.938
Calcium Phosphate Dibasic	41.750mg	26.094
Lecithin thin (light)	3.478mg	2.174
	160.000mg	

Shell:		
Glycerine	19.98mg	19.98
Sorbitol Syrup 70%	27.19mg	27.19
Gelatin	52.83mg	52.83
	100.00mg	
Coat:		
Isomalt	184.667mg	66.7
Sorbitol	92.333mg	33.3
	277.000mg	

The fill compositions in products according to the invention can of course themselves also include flavouring elements to make them more palatable if intended or required to be released in the mouth and additional elements could also be included in the shell composition with the same purpose. However, for products to be swallowed before the fill composition is released, it is of course the flavour of the coating that is of critical importance.

CLAIMS

1. A coated capsule comprising a gelatin shell having a flavoured coating and containing a fill composition, wherein the flavoured coating and the material of the shell include a sugar or a sugar substitute.

2. A coated capsule according to Claim 1 wherein the sugar or sugar substitute in the coating material and the shell is the same.

3. A coated capsule according to Claim 1 or Claim 2 wherein the material of the shell comprises gelatin and a plasticiser in addition to the sugar or sugar substitute.

4. A coated capsule according to Claim 3 wherein the dry composition of the shell material comprises by weight:

Gelatin	33 to 58%
Glycerine	16 to 31%
Sugar or sugar substitute	15 to 30%
Water	up to 15%

5. A coated capsule according to claim 4 wherein the quantity of water in the shell composition is no more than 10% by weight.

6. A coated capsule according to Claim 4 or Claim 5 wherein the ratio of plasticiser (Glycerine + sugar or sugar substitute) to Gelatin in the shell composition is in the range 0.8 to 1.0.

7. A coated capsule according to any of Claims 4 to 6 wherein the ratio of sugar or sugar substitute to Glycerine is in the range 0.8 to 1.2.

8. A coated capsule according to any preceding Claim wherein the sugar or sugar substitute is selected from the group consisting of sorbitol, polyglycerol, mannitol, xylitol, maltitol, isomalt, and corn syrup or mixtures thereof.

9. A coated capsule according to any preceding Claim wherein the flavoured coating comprises an aqueous solution or the sugar or sugar substitute.

10. A coated capsule comprising a gelatin shell having a flavoured coating and containing a breath freshening fill composition.

11. A coated capsule according to any of Claims 1 to 9 wherein the fill composition is a breath freshener.

12. A coated capsule according to Claim 10 or Claim 11 wherein the fill composition comprises parsley seed oil.

INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/GB 98/00916

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K9/48 A61K7/16

According to International Patent Classification(IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61K A23L A23P

Documentation searched other than minimumdocumentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category '	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 283 899 A (ESMOND ANTONY HITCHCOCK) 24 May 1995 cited in the application see page 1, line 13 - page 2, line 10 ---	1,3,8,9
A	WO 95 00123 A (R.P. SCHERER CORPORATION) 5 January 1995 cited in the application see page 8, line 8 - line 32 ---	1,3,8,9
Y	WO 84 03417 A (R.P. SCHERER CORPORATION) 13 September 1984 see page 9, line 5 - line 9 ---	1,3,5, 7-11
Y	EP 0 374 359 A (PHARMACAPS, INC.) 27 June 1990 see page 3, line 19 - line 25 ---	1,3,4, 6-11
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of theInternational search	Date of mailing of the international search report
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Name and mailing address of the ISA	Authorized officer
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PCT/GB 98/00916

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 317 510 A (GREITHER, PETER) 24 May 1989 see the whole document	1,3-11
Y	FR 2 155 286 A (BORGMANN GERHARD) 18 May 1973 see the whole document	1,3-11
A	FR 2 535 608 A (DUBARRY PHILIPPE ET AL.) 11 May 1984 see page 6, line 28 - page 7, line 5 see page 8, line 35 - page 9, line 16	2
A	WO 95 12380 A (PILI, EMANUELE) 11 May 1995 see the whole document	12

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INTERNATIONAL SEARCH REPORT

information on patent family members

Int ional Application No
PCT/GB 98/00916

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 2283899 A	24-05-1995	NONE	
WO 9500123 A	05-01-1995	AU 679755 B	10-07-1997
		AU 6978894 A	17-01-1995
		BR 9406967 A	27-08-1996
		CA 2165783 A	05-01-1995
		DE 69408321 D	05-03-1998
		EP 0706379 A	17-04-1996
		ES 2112547 T	01-04-1998
		JP 8511795 T	10-12-1996
WO 8403417 A	13-09-1984	DE 3307353 A	06-09-1984
		AU 567448 B	19-11-1987
		AU 2690384 A	28-09-1984
		CA 1211712 A	23-09-1986
		EP 0120248 A	03-10-1984
		JP 6017303 B	09-03-1994
		JP 60500623 T	02-05-1985
		US 4744988 A	17-05-1988
EP 374359 A	27-06-1990	US 4935243 A	19-06-1990
		AU 616139 B	17-10-1991
		AU 3811089 A	21-06-1990
		CA 1336499 A	01-08-1995
		JP 2212417 A	23-08-1990
		MX 166393 B	06-01-1993
EP 317510 A	24-05-1989	DE 3869337 A	23-04-1992
FR 2155286 A	18-05-1973	NONE	
FR 2535608 A	11-05-1984	NONE	
WO 9512380 A	11-05-1995	IT 1261861 B	03-06-1996
		AU 8114894 A	23-05-1995